

Retrospective Study of Adrenal Gland Ultrasonography in Dogs with Normal and Abnormal ACTH Stimulation Test

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Abstract

Objective: To identify adrenal ultrasonography parameters that can be used to identify dogs with hypoadrenocorticism.

Design: Retrospective review of adrenal gland measurements and morphology in 56 client-owned dogs presented for a variety of medical reasons suspicious for possible hypoadrenocorticism.

Setting: Private veterinary practice.

Animals: 81 client-owned dogs.

Interventions: Based on adrenal gland measurements and morphology and an ACTH stimulation test, dogs were divided into two groups: hypoadrenocorticism (Group 1, 37 dogs) and a non-hypoadrenocorticism (Group 2, 19 dogs). In addition there was a control group of healthy dogs (Group 3, 25 dogs).

Measurements and Main Results: The median right adrenal length in Group 1-3 was 1.75 cm, 1.8 cm, and 2.03 cm, respectively. Median left adrenal length in Group 1-3 was 1.77 cm, 2.08 cm, and 2.1 cm, respectively. There was no statistically difference between the right and left adrenal gland and within groups. Median right adrenal thickness in Group 1-3 was 0.34 cm, 0.37 cm, and 0.6 cm, respectively. Median left adrenal thickness in Group 1-3 was 0.31 cm, 0.4 cm, and 0.6 cm, respectively. In both right and left measurements, groups 1 and 2 were statistically different from group 3 but there was no statistical difference between groups 1 and 2.

Conclusion and Clinical Relevance: Although not a specific finding, the ultrasound detection of small, flattened, isoechoic adrenal glands should be an alert for possible hypoadrenocorticism, prompting further testing and therapeutic intervention.

Keywords: Hypoadrenocorticism; Addison's disease; Ultrasound; Diagnosis; Canine

Introduction

Hypoadrenocorticism results from the failure of the adrenal glands to secrete adequate quantities of corticosteroids to support normal physiological function. More than 85% of adrenal gland reserve, however, must be lost before clinical signs of hypoadrenocorticism occur and thus bilateral adrenal gland dysfunction is always present in dogs with clinical signs of adrenal failure [1]. The most common cause of hypoadrenocorticism in dogs is primary adrenal failure, which usually results in a deficiency of both glucocorticoids (primarily cortisol) and mineralocorticoids (primarily aldosterone) [1]. Hypoadrenocorticism is regarded as a relatively uncommon disease in dogs, although in certain breeds the disease is heritable with prevalence as high as 10% [2]. In the general dog population, the prevalence of hypoadrenocorticism has been estimated at approximately 0.06- 0.28%, with approximately a 70% female predisposition and a median age of onset of 4 years (range 4 months to 14 years). In the Nova Scotia Duck Tolling Retriever the disease has a younger age of onset [2]. Clinical signs in dogs with hypoadrenocorticism may be either acute or gradual in onset, often wax, and wane with clinical illness sometimes triggered by a stressful event. Clinical signs are typically vague and not pathognomonic and can include a combination of anorexia, vomiting, lethargy/depression, weakness, weight loss, diarrhea, polyuria, polydipsia, and abdominal pain [1]. Abnormalities found on physical examination are also vague and non-specific and can include poor body condition, lethargy, weakness, dehydration, abdominal pain, bradycardia, weak pulses, hypothermia, and decreased capillary refill time [1]. The classic clinicopathologic abnormalities of dogs with hypoadrenocorticism include hyponatremia, hyperkalemia, non-regenerative anemia, and lymphocytosis; however, these changes are not present in all cases and some dogs may show no clinicopathologic abnormalities [1,3,4].

As variable non-specific clinical signs and biochemical changes typify canine hypoadrenocorticism, abdominal ultrasonography is often done as part of the medical work-up. One study stated that there were no characteristic imaging features of primary hypoadrenocorticism in animals and referred to studies in humans where the adrenal glands were often undetected or small in size [5]. To the authors' knowledge there are only two studies in the English veterinary literature that have ultrasonographically evaluated the adrenal gland in dogs with hypoadrenocorticism. In one study of six dogs with hypoadrenocorticism, the range for adrenal gland thickness was 0.22-0.34 cm, whereas in the group of 20 normal control dogs the range was 0.3-0.6 cm [6]. In the other study, 30 dogs with primary hypoadrenocorticism showed significantly thinner adrenal glands and shorter left adrenal gland length. That study concluded that adrenal ultrasonography may be of diagnostic value in dogs with clinical signs suggestive of primary hypoadrenocorticism and that a left adrenal gland measuring less than 0.32 cm in thickness is strongly suggestive of the disease [7]. As abdominal ultrasonography is routinely used in veterinary practice, the purpose of this study was to identify a reliable set of adrenal ultrasonography morphology and measurement parameters that can be used to identify dogs with possible hypoadrenocorticism. An additional purpose of this study was to evaluate a larger population of dogs with hypoadrenocorticism and to compare the adrenal glands of these dogs to those of dogs that were initially suspected to have hypoadrenocorticism on clinical examination, biochemical changes, and ultrasonography but subsequently ruled out by means of the ACTH stimulation test.

Materials and Methods

This was a retrospective study in which the records of 56 privately owned dogs that had both an abdominal ultrasonography and an ACTH stimulation test performed were evaluated. To exclude inter-observer bias, all adrenal gland measurements and morphology were retrospectively reviewed using both still and video clips by one person (EL) and correlated with clinical signs, biochemical changes, and results of an ACTH stimulation test.

Adrenal gland size and morphology was evaluated by abdominal ultrasound examination using an 8 MHz probe and an ultrasound machine^[a]

Adrenal gland morphology was subjective and based on intrinsic adrenal gland structure, namely: the gland's echogenic appearance compared to the surrounding fat; echogenic separation between gland, echogenic capsule and surrounding fat; and contour of the gland. With the patient in right lateral recumbency, the left adrenal gland was identified by approaching the aorta in the long axis from a left lateral approach at the level of the left renal artery. The left adrenal gland was identified in its normal position cranial to the left renal artery, adjacent to the aorta, and medial to the left kidney within 5 cm of depth in order to ensure adequate image resolution. The right adrenal gland was approached with the patient in the same right lateral recumbency but then tilted 45 degrees toward dorsal recumbency to allow the scanning hand to be placed close enough to the spine from a right lateral approach.

The right adrenal gland was imaged by approaching the right kidney in long axis, applying manual pressure with the scanning hand to arrive at a long axis image of the caudal vena cava and aorta at the level of the right renal artery. From this position, while displacing the ascending and transverse colon medially with scanning hand pressure, the sonographer retracted the probe until the right adrenal was imaged in its location between the vena cava and aorta. The same 5 cm depth limit was used to ensure adequate resolution for identification and measurement. Following the morphological evaluation of the adrenal glands, measurements were done using electronic calipers. The maximum length of each adrenal gland was measured in the longitudinal plane and the maximum thickness was measured at the greatest dorso-ventral dimension and assessed as a single measurement made perpendicular to the long axis. Only precise measurements taken from images with clear adrenal gland resolution were entered into the study. The dogs were divided into three groups: Group 1 consisted of 37 dogs with clinical signs and serum biochemistry changes and/or an ultrasonography appearance of their adrenal glands that was suspicious of hypoadrenocorticism and confirmed on an ACTH stimulation test. Group 2 consisted of 19 dogs with clinical signs and serum biochemistry changes and/or an ultrasonography appearance of their adrenal glands that was suspicious of hypoadrenocorticism but ruled out by a normal ACTH stimulation test. Group 3 consisted of 25 healthy normal dogs that had no clinical signs or biochemical evidence of hypoadrenocorticism and a normal sonogram appearance of their adrenal glands. The ACTH stimulation test was done according to standard protocol – blood samples collected at baseline and 60 minutes after intra-muscular injection of 250 µg/dog. Hypoadrenocorticism was diagnosed if the pre- and post-ACTH cortisol was less than 2 µg/dL. Dogs in group 2 showed a normal ACTH stimulation test response (post-ACTH cortisol > 5 µg/dL). Any dogs with an ACTH stimulation test within the grey-zone (2- 5µg/dl) or a history of corticosteroid therapy were excluded from the study.

Data analysis

All data were tabulated in a spreadsheet program^[b] and statistical analysis was performed with the aid of a statistical software package.^[c] Descriptive statistics were used to describe the data. For single parameters (age, bodyweight, adrenal length, and adrenal thickness), differences between the groups were tested using one-way analysis of variance with Bonferroni and Tukey-Kramer comparisons. The data was normally distributed and the level of significance was set at $p < 0.05$. Within each group, correlations between bodyweight and age and length and width of the adrenal glands were tested using the Spearman's rank-order correlation coefficient.

Results

The median age in Group 1 was 7 years (range 1-14 years); Group 2, 8 years (range 1-11 years); and Group 3, 11 years (range 3-14 years), with group 3 being statistically older than the other two groups. A similar sex distribution was present within the three groups. The median weight in Group 1 was 24 kg (range 4-65 kg); Group 2, 18 kg (range 8-35 kg); and Group 3, 18 kg (range 8-35 kg), with no statistical difference between the groups.

Diseases reported in group 2 included gastrointestinal (8), CNS (1), renal failure (1), urinary tract infection (1), and non-specific disease(8). None of the diseases were deemed to be of a severe critical nature.

The adrenal glands in group 1 were subjectively found to be flattened in contour, largely isoechoic to mildly hypoechoic to the surrounding fat (Figure 1),

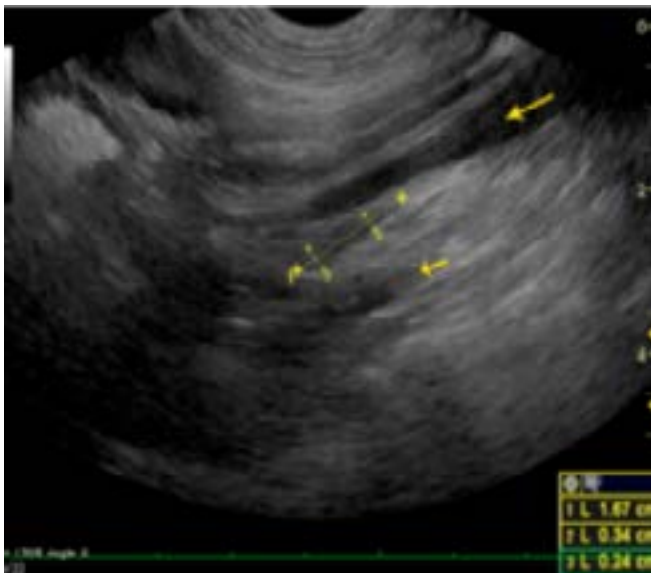


Figure 1: Ultrasound image of the left and right adrenal glands from a dog with hypoadrenocorticism. Both glands appear flattened in contour and largely isoechoic to mildly hypoechoic to the surrounding fat. Subnormal widths (left 0.38 and 0.37 cm, right 0.34 and 0.24 cm) are evident on measurements. Large arrow indicates caudal vena cava and shorter arrow the aorta respectively used as landmarks for the right adrenal gland.

and showed loss of cortico-medullary detail. Subjective change in gland length compared to a normal adrenal gland (Figure 2) did not appear to be a common finding by the interpreter. The adrenal glands in group 2 subjectively were interpreted to have similar morphological parameters compared to group 1 with regards to comparative echogenicity and flattened glandular contour. In both groups 1 and 2, the adrenal glands were not readily recognized with a distinct echogenic separation between gland, echogenic capsule, and surrounding fat



Figure 2: Ultrasound image of the left adrenal gland from a normal dog (group 3) demonstrating normal size, rounded contour, and distinct hypoechoic parenchyma compared to surrounding fat.

despite proper sonographic positioning, adequate imaging window, and a scanning depth of less than 5 cm. All dogs in groups 1 and 2 showed a varying degree of presence of the subjective parameters evaluated - flattened contour, tendency toward isoechogenicity to surrounding fat.

The median right adrenal length in group 1 was 1.75 cm (range 1.22-3.28 cm); in group 2, 1.8 cm (range 1.24-3.79 cm); and in group 3, 2.03 cm (range 1.2-2.96 cm); with no group showing statistical difference (Figure 3). The median left adrenal length in group 1 was 1.77 cm (range 0.9-3.4 cm); in group 2, 2.08 cm (range 1.35-3.5 cm); and in group 3, 2.1 cm (range 1.3-3.2 cm); with no group showing a statistical difference (Figure 4).

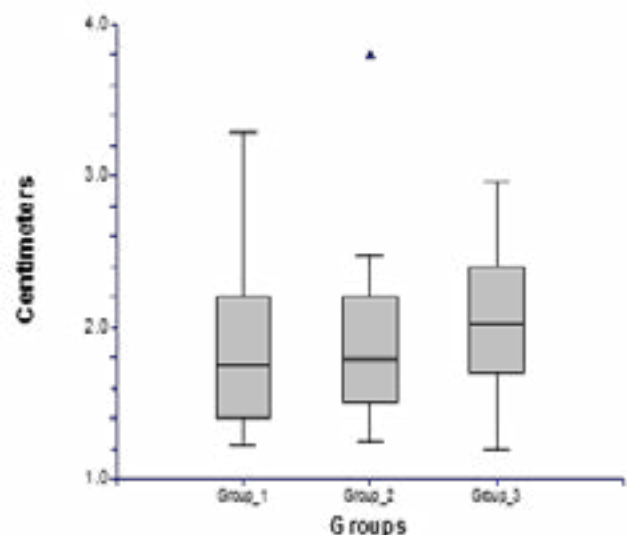


Figure 3: Right adrenal length. Data shown as median (horizontal line within box), 25th and 75th percentiles (horizontal ends of boxes), and 10th and 90th percentiles (T-bars). Black triangle represents an outlier. Group 1 = hypoadrenocorticism; Group 2 = non-hypoadrenocorticism; Group 3 = control. There was no statistical difference between the groups.

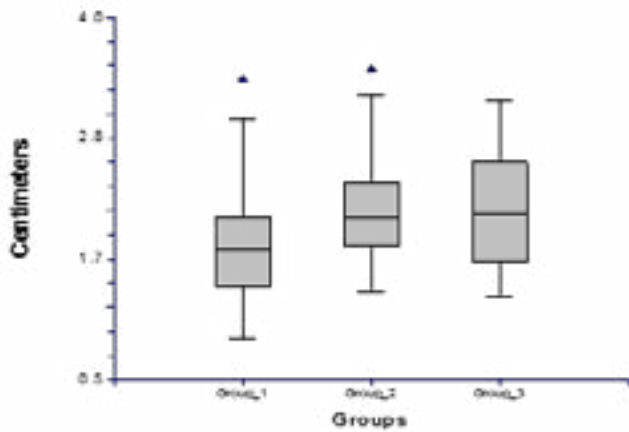


Figure 4: Left adrenal length. Data shown as median (horizontal line within box), 25th and 75th percentiles (horizontal ends of boxes), and 10th and 90th percentiles (T-bars). Black triangles represent outliers. Group 1= hypoadrenocorticism; Group 2 = non-hypoadrenocorticism; Group 3 = control. There was no statistical difference between the groups.

The median right adrenal thickness in group 1 was 0.34 cm (range 0.18-0.48 cm); in group 2, 0.37 cm (range 0.12-0.58 cm); and in group 3, 0.6 cm (range 0.4-0.82 cm); with groups 1 and 2 showing statistical difference from group 3 (Figure 5). There was, however, no statistical difference between groups 1 and 2. The median left adrenal thickness in group 1 was 0.31 cm (range 0.16-0.5); in group 2, 0.4 cm (range 0.25-0.6); and in group 3, 0.6 cm (range 0.4-1.2); with groups 1 and 2 showing a statistical significant difference from group 3 (Figure 6). There was, however, no statistical difference between groups 1 and 2. Within all groups, no correlation could be shown between the bodyweight and the length and thickness of the adrenal glands, nor between age and the length and thickness of the adrenal glands.

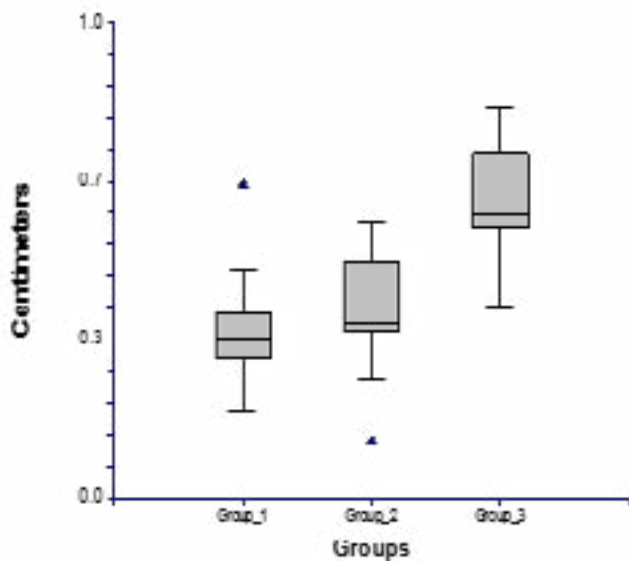


Figure 5: Right adrenal thickness. Data shown as median (horizontal line within box), 25th and 75th percentiles (horizontal ends of boxes), and 10th and 90th percentiles (T-bars). Black triangles represent outliers. Group 1= hypoadrenocorticism; Group 2 = non-hypoadrenocorticism; Group 3 = control. Groups 1 and 2 were statistical different ($p < 0.05$) from group 3 but not between each other.

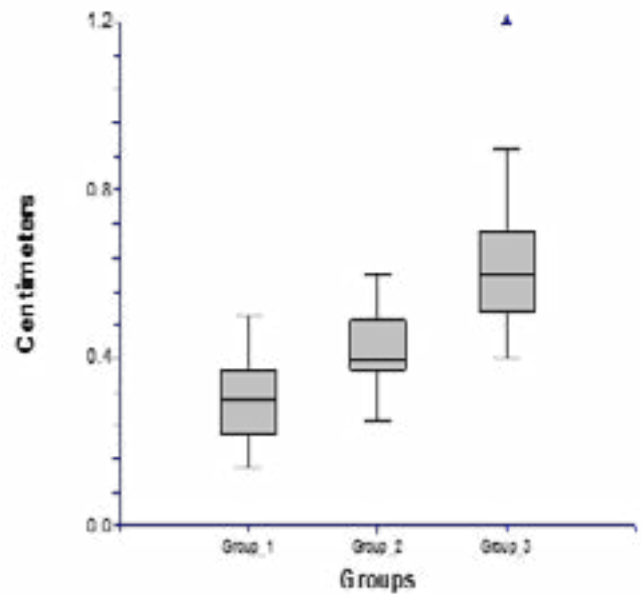


Figure 6: Left adrenal thickness. Data shown as median (horizontal line within box), 25th and 75th percentiles (horizontal ends of boxes), and 10th and 90th percentiles (T-bars). Black triangle represents an outlier. Group 1= hypoadrenocorticism; Group 2 = non-hypoadrenocorticism; Group 3 = control. Groups 1 and 2 were statistical different ($p < 0.05$) from group 3 but not between each other.

Discussion

Hypoadrenocorticism can be a life-threatening and possibly fatal disease if not treated immediately [1,4]. Although a tentative diagnosis can be made on clinical signs and laboratory findings, a definitive diagnosis can only be made on an ACTH stimulation test, aldosterone to renin ratio, and/or the cortisol to ACTH ratio. Unfortunately, typical clinical signs and laboratory findings are not evident in all cases and the definitive laboratory test results are usually not immediately available. As ultrasonography is widely used and results immediately available, it would be ideal as a diagnostic aid for hypoadrenocorticism. The two previous studies in dogs with hypoadrenocorticism have shown a measurable reduction in size of the adrenal glands on ultrasound examination with occasionally the adrenal glands not being visualized [6,7].

The study by Hoerauf [6], where the adrenal glands were measured in six dogs with hypoadrenocorticism, showed that the left adrenal length and thickness to range from 1-1.97 cm and 0.22-0.3 cm, respectively; and the right adrenal length and thickness to range from 0.95-1.88 cm and 0.22-0.34 cm, respectively. There was also a statistical reduction in size of the left adrenal gland in the dogs with hypoadrenocorticism compared to the left adrenal gland in normal dogs. In this current study, there was no statistical difference in the length of the adrenal gland between the groups but there was a statistical difference with the thickness of both adrenal glands in dogs with hypoadrenocorticism and the control group but no statistical difference between dogs with hypoadrenocorticism and those with other diseases. In the study by Wenger [7] the adrenal glands of 30 dogs with hypoadrenocorticism were measured and compared with 14 healthy dogs and 10 dogs with diseases mimicking hypoadrenocorticism. Dogs with hypoadrenocorticism had significantly thinner adrenals compared with the other two groups, and their left adrenal glands were significantly shorter than those of healthy dogs. The study concluded that adrenal ultrasonography may be of diagnostic value in dogs with clinical signs suggestive of hypoadrenocorticism, and a left adrenal gland measuring less than 0.32 cm in thickness was strongly suggestive of the disease. These studies support that adrenal gland thickness appears to be most important factor in the interpretation of adrenal disease. A similar narrowed thickness was found in both adrenal glands of dogs with hypoadrenocorticism in this current study. In this current study, although both the left and right adrenal length in dogs with hypoadrenocorticism was shorter than dogs with non-adrenal disease and control dogs it was not a statistically significant change. Both the left and right adrenal gland thickness in dogs with hypoadrenocorticism was statistically smaller than control dogs but not different from dogs with non-adrenal disease. However, the adrenal glands of dogs with hypoadrenocorticism tended to show the smallest thickness. On ultrasound, dogs without any overt evidence of adrenal gland disease showed a left adrenal gland length range of 10.7- 50.2 mm and a caudal polar width range of 1.9-12.4 mm; and a right adrenal gland length range of 10-39.3 mm and caudal polar width range of 3.1-12 mm [8]. The right adrenal measurements are similar to the control groups in this study; however, the left adrenal measurements are larger than the controls in this study. In the dog, correlations between adrenal gland size and body weight has been reported [7-9] and between adrenal gland size and age [8]. In this current study there were no correlations between adrenal gland size and body weight and between adrenal gland size and age. In dogs given long-term exogenous glucocorticoids the ultrasonography appearance of their adrenal glands was a decreased height of the cranial and caudal pole and length of entire gland but the degree of atrophy varied between individuals [10]. In this current study both the dogs with hypoadrenocorticism and those with other diseases showed small, flattened, isoechoic adrenals on ultrasonography. However, in the dogs with hypoadrenocorticism, adrenal cortico-medullary detail appeared to be obscured,

which can be ascribed to the lack of or diminished glandular activity within the cortex. Less secretory activity of the cortex would theoretically cause diminished fluid accumulation in the cells rendering the cortex more hyperechoic than normal causing diminished the contrast between medulla and cortex and surrounding fat. Inter- and intra-observer variability can be relevant in the ultrasonography measurement of the adrenal glands [7]. In this study, inter-observer variability was excluded as both the morphology and measurements were reviewed by the same person using the same technique.

In a previous study, small adrenal glands were also reported in a group of dogs without hypoadrenocorticism [7]. Final diagnoses for dogs in that group were: acute gastroenteritis, neoplasia, renal disease, hypothyroidism, and urinary tract infection. Similar diseases were evident in this current study, which also resulted in the finding of small adrenal glands on ultrasonography. As in the study of Wenger, [7] the ACTH stimulation test was normal in each of the dogs in this group, making adrenal atrophy secondary to corticosteroid administration unlikely. It can be speculated that the finding of small adrenals in the non-hypoadrenocorticism group could be due to loss of reserve due to stress. The syndrome of critical illness-related corticosteroid insufficiency is characterized by an inadequate production of cortisol in relation to an increased demand during periods of severe stress, particularly in critical illnesses [11]. Relative adrenal insufficiency appears to be acquired secondary to the stress of sepsis, shock, trauma, or surgery [12]. Substances released in response to illness or injury may impair the synthesis of cortisol via inhibitory actions on the hypothalamic-pituitary axis and can result in corticotropin resistance and/or altered cortisol metabolism, which may subsequently reduce the size of the adrenal gland. Dogs with babesiosis had a median ACTH concentration significantly lower than controls dogs [13]. This may result in a reduction in adrenal gland size, due to the syndrome of critical illness-related corticosteroid insufficiency. There are, however, no reported adrenal ultrasound findings in dogs with babesiosis or with relative adrenal insufficiency.

Conclusion

This study suggests that the ultrasonography finding of small (around 0.3 cm in thickness), flattened, isoechoic adrenals that are difficult to locate despite adequate scanning window and position are useful in the support of a suspicion of primary hypoadrenocorticism but unfortunately not diagnostic as similar changes can occur with other disease conditions. This finding should, however, prompt additional adrenal function testing. A possible limitation of the study is the relatively small numbers of dogs that had clinical signs and/or an ultrasonography appearance of adrenal glands that were suspicious of hypoadrenocorticism but subsequently ruled out by a normal ACTH stimulation test.

Footnotes

^aGeneral Electric Logic E ultrasound machine, GE Healthcare Biosciences, Box 643065 Pittsburgh, USA.

^bExcel®, Microsoft Corporation.

^cNCSS®, 329 North 1000 East, Kaysville, Utah, USA.

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